IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re the application of:
Erwin MATTES and Peter H. MATTHIESSEN

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National Phase of PCT/AT98/00130
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For: *Alpha 1-Antitrypsin Preparation and Method for the Production Thereof*

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By: Carmen Parra
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PRELIMINARY AMENDMENT

Dear Sir:

Please amend the above-identified patent application as follows:

In the claims:

Cancel claims 1-9; and add new claims 10- 56 as follows:

WHAT IS CLAIMED IS:

10. A native, chromatographically purified αl-AT preparation comprising at least the isomer having a pI value of between 4.3 and 4.4, having a purity of at least 0.7 PU/mg of

protein and a relative plasma αl-AT activity of at least 120% with a portion of inactive αl-AT of less than 10%.

11. A preparation as set forth in claim 10, said preparation being provided as a pharmaceutical preparation.

12. A preparation as set forth in claim 10, said preparation having been purified from a plasma pool.

13. A preparation as set forth in claim 10, wherein said purity is more than 0.9 PU/mg of protein.

14. A preparation as set forth in claim 13, wherein said purity is more than 1.0 PU/mg of protein.

15. A preparation as set forth in claim 13, wherein said purity is more than 1.1 PU/mg of protein.

16. A preparation as set forth in claim 13, wherein said purity is more than 1.2 PU/mg of protein.

17. A preparation as set forth in claim 10, wherein said portion of inactive αl-AT is less than 5%.

18. A preparation as set forth in claim 17, wherein said portion of inactive αl-AT is less than 2%.

19. A preparation as set forth in claim 10, said preparation being free from inactive αl-AT.

20. A preparation as set forth in claim 10, wherein said αl-AT is a preservative αl-AT.

21. A preparation as set forth in claim 10, said preparation having an isomer distribution of said α1-AT corresponding to the isomer distribution of the native protein.

22. A preparation as set forth in claim 21, wherein said isomer distribution of said α1-AT corresponds to a quadruplet band pattern visible at isoelectric focusing.

23. A preparation as set forth in claim 10, said preparation having been treated for an inactivation of pathogens possibly present.

24. A preparation as set forth in claim 10, said preparation being provided in storage-stable form.

25. A preparation as set forth in claim 24, said preparation being provided as a lyophilisate.

26. A preparation as set forth in claim 24, said preparation being provided as a solution.

27. A preparation as set forth in claim 26, wherein said solution is suitable for one of an i.v. administration, an aerosol and a spray.

28. A preparation as set forth in claim 10, said preparation being provided in association with at least one of liposomes, phospholipids and other microparticulate and nanoparticulate formulations.

29. A method of producing a native α1-AT preparation having at least an isomer with a pI value of between 4.3 and 4.4, having a purity of at least 0.7 PU/mg of protein and a relative plasma α1-AT activity of at least 120% with a portion of inactive α1-AT of less than 10%, said method comprising providing a starting material containing active and inactive α1-AT, providing a chromatographic material suitable for adsorption chromatography, passing said α1-AT-containing starting material over said

chromatographic material so as to adsorb said active αl-AT on said chromatographic material so as to purify said αl-AT, and eluting said purified active αl-AT in a fraction.

30. A method as set forth in claim 29, wherein said starting material is selected from a plasma and a plasma fraction.

31. A method as set forth in claim 30, wherein said starting material is an albumin-depleted plasma fraction.

32. A method as set forth in claim 30, wherein said starting material is a Cohn V precipitate.

33. A method as set forth in claim 31, further comprising prepurifying said plasma fraction.

34. A method as set forth in claim 29, wherein said chromatographic material suitable for adsorption chromatography is an inorganic chromatographic material.

35. A method as set forth in claim 34, wherein said inorganic chromatographic material is hydroxyapatite.

36. A method as set forth in claim 35, wherein said hydroxylapatite is a ceramic hydroxylapatite.

37. A method as set forth in claim 29, wherein said chromatographic material suitable for adsorption chromatography is an anion exchanger.

38. A method as set forth in claim 37, further comprising providing a detergent, said adsorption chromatography on said anion exchanger being effected in the presence of said detergent.

39. A method as set forth in claim 37, wherein said anion exchanger is Q-Sepharose.

40. A method as set forth in claim 29, further comprising providing a buffer free of mercaptoethanol, said adsorption chromatography being effected by using said buffer.

41. A method as set forth in claim 29, further comprising providing a buffer having a pH of between 5.5 and 8.0 and using said buffer during eluting of said active α1-AT in a fraction.

42. A method as set forth in claim 41, wherein said buffer used during eluting has a pH of about 6.5-6.8.

43. A method as set forth in claim 41, wherein said buffer used during eluting comprises a salt having an ionic strength corresponding to 60 mM of phosphate.

44. A method as set forth in claim 41, wherein said buffer used during eluting comprises a salt having an ionic strength corresponding to 40 mM of phosphate.

45. A method as set forth in claim 41, wherein said buffer used during eluting comprises a salt having an ionic strength corresponding to 50 to 130 mM of sodium chloride.

46. A method as set forth in claim 29, further comprising a further step selected from the group consisting of precipitation, filtration, gel filtration, treatment with an inorganic carrier material and chromatographic purification.

47. A method as set forth in claim 29, wherein said adsorption chromatography is carried out on an anion exchanger in combination with an adsorption on hydroxylapatite.

48. A method as set forth in claim 47, wherein said adsorption chromatography is carried out in the presence of a detergent.

49. A method as set forth in claim 29, wherein one single adsorption chromatography is carried out.

50. A method as set forth in claim 49, further comprising a further purification step other than an adsorption chromatography.

51. A method as set forth in cl aim 29, further comprising recovering a protein selected from the group of transferrin, albumin, orosomucoid and apolipoprotein in a further fraction.

52. A method as set forth in claim 29, further comprising a step for inactivating any pathogens possibly present.

53. A method as set forth in claim 52, wherein said step for inactivating possibly present pathogens is a treatment with at least one of a detergent, a solvent and heat.

54. A method as set forth in claim 29, wherein eluting is effected such that the αl-AT-containing fraction also comprises the isomer having a pI value of between 4.3 and 4.4.

55. A method of separating active αl-AT from inactive αl-AT, said method comprising providing a carrier material and employing said carrier material for said separating of active αl-AT from said inactive αl-AT.

56. A method as set forth in claim 55, wherein said carrier material is an inorganic carrier material.

57. A method as set forth in claim 56, wherein said inorganic carrier material is hydroxylapatite.

58. A method as set forth in claim 57, wherein said hydroxylapatite is ceramic hydroxylapatite.

Applicants submit that the claims being added in the preliminary amendment and the specification are in compliance with all patentability requirements. Applicants therefore respectfully request that the claims be allowed. To expedite allowance, the Examiner is encouraged to contact Applicants' attorney at the number provided below.

Respectfully submitted,
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